IOMED

February 2, 2005

Division of Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. 2000N-1409
Comments – Proposed Rule (*Federal Register* 69:64313, November 4, 2004)

Dear Sir/Madam:

Iomed, Inc. is a developer and manufacturer of iontophoresis devices. As such, we are affected by the issues regarding the classification of these devices. This letter is intended as a response to the November 4, 2004 request for comments published in the Federal Register. In this publication, FDA requested information about the safety and efficacy of iontophoresis devices so that the reclassification of those devices (from class III to class II) can be considered.

Class II comprises devices for which general controls (considered appropriate for Class I devices) are determined to be insufficient to provide reasonable assurance of safety and effectiveness. Class II devices must comply with general controls as well as any special controls established for these devices such as performance/design standards or guidelines. Other special controls may include postmarketing surveillance, patient registries, or other appropriate action that FDA deems necessary to provide reasonable assurance of a device's safety and effectiveness.

Class III devices are those where there is insufficient information to determine the adequacy of general controls, performance standards or special controls in providing reasonable assurance of safety and effectiveness. Generally, Class III devices are those that are to be used for life-sustaining or life-supporting purposes, those implanted in the human body, and those presenting potential unreasonable risk of illness or injury. These devices require premarket approval to achieve adequate regulatory control.

The goal of this response is to show that there is sufficient information to determine the adequacy of general controls, design controls, performance standards and/or guidance documents. It is Iomed's belief that these controls are sufficient to provide reasonable assurance of safety and efficacy.

***Iontophoresis***

Iontophoresis is a noninvasive drug delivery option that employs a direct electrical current to introduce ions of soluble salts or other drugs into the body. Iontophoresis technology is based on the principle that an electric potential will cause ions in solution to migrate according to their

electrical charges. In practice, an ionic drug is propelled by an electric field across intact skin and into underlying tissue. Ions are transferred at a rate proportional to the magnitude of the current flow. In addition, the quantity and distribution of a drug delivered into and across the skin by iontophoresis is dependent on the charge and molecular weight of the ion, duration of current flow and other factors.

***Effectiveness of Iontophoresis***

The effectiveness of iontophoresis is well established in literature and practice. It is based on chemical properties of drugs, material science, pharmacokinetics and the physics of ion transfer. Effectiveness of iontophoretic delivery has been clinically proven for drugs such as lidocaine and epinephrine and most recently fentanyl. Pilocarpine is another drug known to be successfully delivered by iontophoresis.

Pre-amendment iontophoresis devices are known to exist. These devices used pilocarpine (for diagnosis of cystic fibrosis), lidocaine and epinephrine (for anesthetizing the intact tympanic membrane) and fluoride (applied to the teeth for reduction of sensitivity and cavity prevention). During original classification panel meetings, other well-known pre-amendment device uses were discussed, including the administration of corticosteroids.

***Safety of Iontophoresis***

The safety of iontophoresis is well understood. Risks identified by the Physical Medicine Device, the Ear, Nose and Throat Device and the Dental Device Classification Panels, FDA Advisory Committees identified the following:

- Electrical Shock caused by excessive leakage current or device malfunction;
- Burns resulting from high current over time;
- Cardiac arrest caused by excessive electrical current passing through the heart; and
- Inappropriate therapy resulting from inaccurate current measurement.

The FDA concluded that iontophoresis devices present the risk of electrical shock and that measurement limitations inherent in the use of these devices should be controlled. FDA issued a proposed regulation classifying iontophoresis devices for specialized uses as Class II and for all other uses into Class III. These classifications were confirmed with some modifications in the final rule published in 1983. In the preamble to the final rule, FDA emphasized that iontophoresis devices are able to deliver systemically active medications that may be harmful because the dosage level administered to the patient is unpredictable.

IEC 479-1, *Effects of Current on Human Beings and Livestock*, shows that DC currents from 2mA to 20 mA usually cause no harmful physiological effects regardless of the total time of exposure. Contemporary design of iontophoresis power supplies using low-voltage, battery-powered, microprocessor controlled current sources which limit output to 5 milliamperes or less has eliminated as far as possible the probability of cardiac arrest or serious injury from electrical shock. The possibility of interference with electrically sensitive support systems, e.g., pacemakers, remains, and use of iontophoresis devices in patients with such systems should be contraindicated.

Iontophoresis electrode designs and materials can incorporate features that take into consideration appropriate electrochemistry, current density, and drug compatibility, together with the power supply features mentioned above. These measures provide a means of standardizing the rate of delivery for a particular iontophoresis system and minimize the risk of skin irritation resulting from excessive electric current or lack of pH control. Contemporary iontophoresis devices use microprocessors to increase reliability, to control current output and total delivered charge. These controls provide assurance of safe, consistent and accurate dosing. Such devices have also been designed to incorporate a safety feature that terminates delivery of electrical current when impedance rises above a preset threshold.

Incidence of skin irritation can be reduced by providing adequate instructions for use emphasizing the importance of proper skin site selection, preparation (cleaning) and proper application of the iontophoretic electrodes.

The above mentioned precautions have minimized or eliminated safety related issues by the design of Iomed's product line. Product design is complemented by the labeling, including the instructions for use, warnings, contraindications and precautions. The combination of design and labeling provides a device that is safe for use in medical practice.

***Benefits of Iontophoresis***

Iontophoretic drug delivery systems may be used to deliver water-soluble ionic medicaments for systemic or local applications. Iontophoresis offers unique benefits over other more invasive drug delivery methods. In the specific case of using pilocarpine for the diagnosis of cystic fibrosis, iontophoresis is the only effective delivery method. Delivery of water-soluble ionic medicaments via iontophoresis can significantly improve safety, since it is a non-invasive delivery system and therefore avoids the risks associated with more invasive delivery methods.

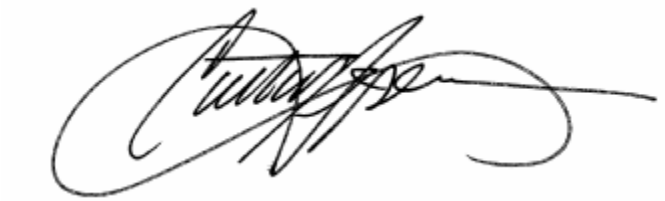
***Conclusion***

Design of iontophoresis devices is at a technological stage such that system safety and use can be controlled, and any risks of injury from excess current, electric shock or pH changes can be minimized. Contraindications and risks of iontophoresis are known, and information can be placed in the product and/or drug labeling to instruct the medical practitioner on patient selection, site preparation, device/drug use and potential side effects. This knowledge, when communicated and used properly, makes iontophoresis devices safe and effective. This, in addition to the fact that iontophoresis provides benefits over other, more invasive drug delivery methods and makes iontophoresis an attractive option for the medical community.

Iontophoresis devices do not pose a high risk to patients, as they are not used as life-sustaining or life-supporting devices. In addition, they are not implanted in the body and do not present a potential unreasonable risk of illness or injury. The risks are known, minor and rare, and can be minimized by employing design controls and risk analysis.

Iontophoresis devices can be reasonably placed in Class II. Enough is understood to determine the adequacy of general controls and performance standards to provide reasonable assurance of safety and effectiveness.

Respectfully,



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